

CLAIMS

1. (Original) A method of treating a solid tumour in a subject, the method comprising the following steps

- (i) delivering to the solid tumour a composition comprising an engineered ovine atadenovirus and a lipid; and
- (ii) administering a prodrug to the subject,

wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts the prodrug to a cytotoxic metabolite, the gene being under the control of the promoter.

2. (Original) A method as claimed in claim 1 in which the promoter is selectively active in a specific tissue.

3. (Amended) A method as claimed in claim 1 ~~or claim 2~~ in which the solid tumour is prostate cancer.

4. (Amended) A method as claimed in claim ~~2 or claim 3~~ 1 in which the specific tissue is prostate tissue.

5. (Amended) A method as claimed in ~~any one of claims 1 to 4~~ in which the promoter is a prostate specific membrane antigen promoter.

6. (Amended) A method as claimed in ~~any one of claims 1 to 5~~ in which the promoter is a probasin promoter.

7. (Amended) A method as claimed in ~~any one of claims 1 to 6~~ in which the ovine atadenovirus further comprises a transcriptional enhancer element.

8. (Original) A method as claimed in claim 7 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.

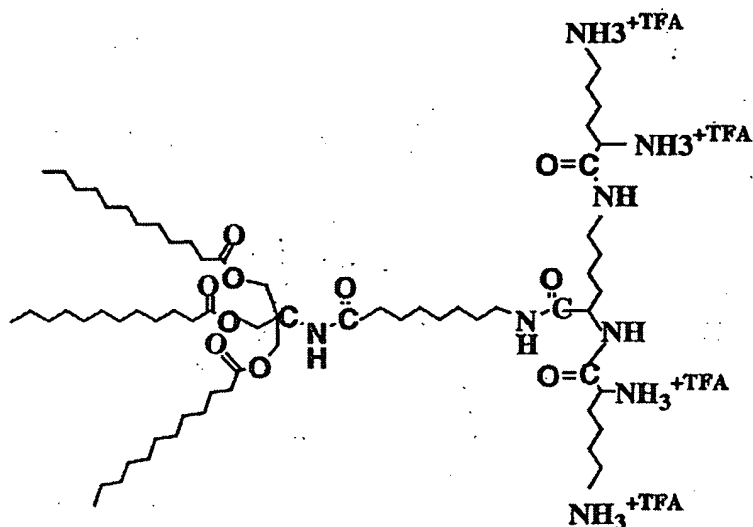
9. (Amended) A method as claimed in ~~any one of claims 1 to 8~~ in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase/5-fluorocytosine, human cytochrome P450/cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-fluorouridine, cytosine kinase/cytosine arabinoside, *E. coli*/GPT/ 6-thioxanthine, *E. coli* nitroreductase/5(-aziridine-1-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/ 6-methylpurine-2-deoxyriboside or fludarabine.

10. (Amended) A method as claimed in ~~any one of claims 1 to 8~~ in which the enzyme is a purine nucleoside phosphorylase (PNP) and the prodrug is a purine prodrug which is converted by PNP to a toxic purine metabolite.

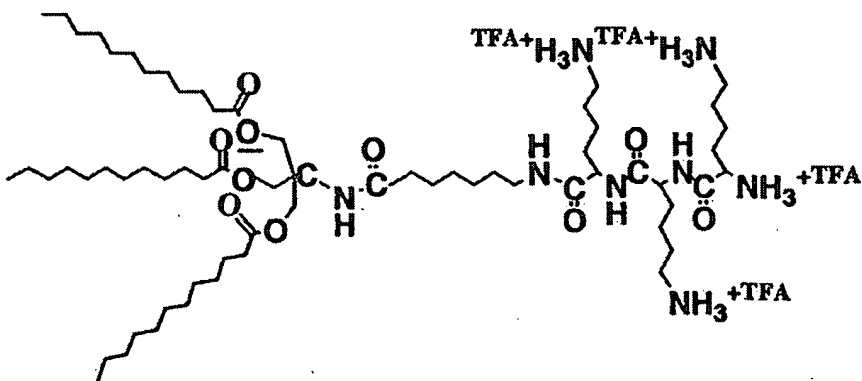
11. (Original) A method as claimed in claim 10 in which the prodrug is 6-methyl purine-2-deoxyriboside (6MPDR) or fludarabine.

12. (Amended) A method as claimed in ~~any one of claims 1 to 11~~ in which the lipid is a cationic lipid.

13. (Amended) A method as claimed in ~~any one of claims 1 to 12~~ in which the lipid is CSO87 having the formula :



14. (Amended) A method as claimed in ~~any one of claims 1 to 12~~ which the lipid is CSO60 having the formula:



15. (Amended) A method as claimed in ~~any one of claims 1 to 6~~ in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.

16. (Original) A composition comprising

- (i) an engineered ovine atadenovirus; and
- (ii) a lipid,

wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts a prodrug to a cytotoxic metabolite, the gene being under the control of the promoter.

17. (Original) A composition as claimed in claim 16 in which the promoter is selectively active in a specific tissue.

18. (Amended) A composition as claimed in claim 16 ~~or claim 17~~ in which the promoter is a prostate specific membrane antigen promoter.

19. (Amended) A composition as claimed in ~~any one of~~ claims 16 ~~to 18~~ in which the promoter is a probasin promoter.

20. (Amended) A composition as claimed in ~~any one of~~ claims 16 ~~to 19~~ in which the ovine atadenovirus further comprises a transcriptional enhancer element.

21. (Original) A composition as claimed in claim 20 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.

22. (Amended) A composition as claimed in ~~any one of~~ claims 16 ~~to 21~~ in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase/5-fluorocytosine, human cytochrome P450/ cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-fluorouridine, cytosine kinase/cytosine arabinoside, *E. coli* GPT/ 6-

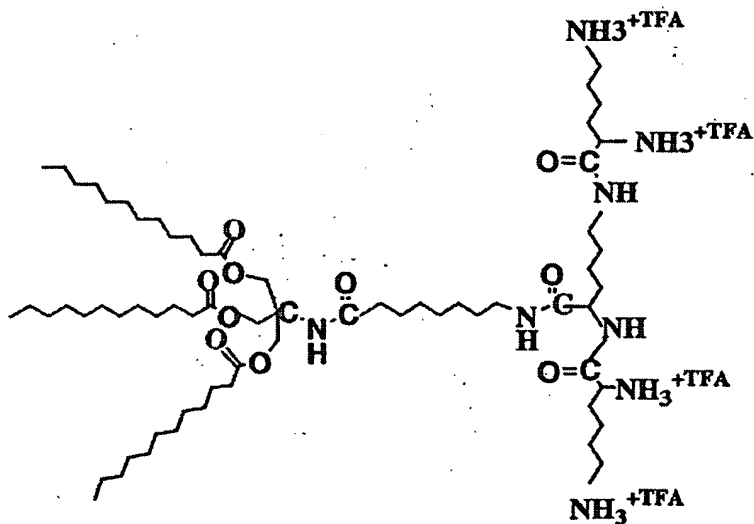
thioxanthine, *E. coli* nitroreductase/5(-aziridine-1-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/6-methylpurine-2-deoxyriboside or fludarabine.

23. (Amended) A composition as claimed in ~~any one of claims 16 to 21~~ in which the enzyme is a purine nucleoside phosphorylase (PNP) and the prodrug is a purine prodrug which is converted by PNP to a toxic purine metabolite.

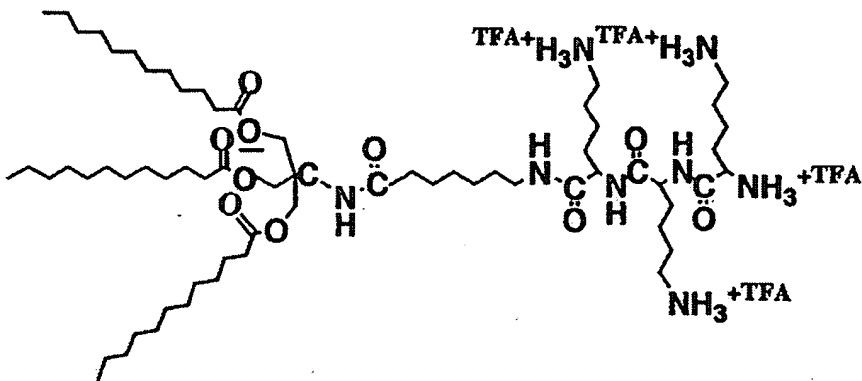
24. (Original) A composition as claimed in claim 23 in which the prodrug is 6-methyl purine-2-deoxyriboside (6MPDR) or fludarabine.

25. (Amended) A composition as claimed in ~~any one of claims 16 to 24~~ in which the lipid is a cationic lipid.

26. (Amended) A composition as claimed in ~~any one of claims 16 to 25~~ in which the lipid is CSO87 having the formula :



27. (Amended) A composition as claimed in ~~any one of~~ claims 16 to 25 in which the lipid is CSO60 having the formula:



28. (Amended) A composition as claimed in ~~any one of~~ claims 16 to 27 in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.